C2 consisting of *Arabidopsis*, maize, wheat, rice, soybean, tomato, tobacco, carrots, potato, sugar beets, sunflower, yam, rape seed, and petunia.

REMARKS

Claims 8-10, 14, 15, and 21-26 are pending and under active consideration. Claims 9 and 26 have been amended to correct typographical errors. A marked version of the claims indicating the changes to the claims is attached hereto as Appendix A. A copy of the claims as pending is attached hereto as Appendix B. The amendments are fully supported by the present specification as mentioned below, and do not represent new subject matter.

1. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, FOR INDEFINITENESS IS AVOIDED AND SHOULD BE WITHDRAWN

Claims 9, 10, 14, 15, and 26 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner has pointed out that Claim 9 comprises two independent sentences. The Examiner also has pointed out that Claim 26 is indefinite for the recitation of the term "transgennic."

Applicants have amended Claim 9 to recite "wherein" after the first comma in line 1, as suggested by the Examiner. Claim 26, has been amended to replace "transgennic" and recite the correct spelling of the term "transgenic."

Applicants have amended claims 9 and 26. In view of the forgoing amendments, Applicants respectfully submit that the rejection is avoided and request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

2. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR ENABLEMENT SHOULD BE WITHDRAWN

Claims 8-10, 14, 15, and 21-26 26 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification, while admitted to be enabling for transgenic plants comprising a transfected gene encoding either glutamine synthase (GS) or aspartate synthetase (AS), is alleged not to provide enablement for transgenic plants comprising a transfected gene encoding aspartate aminotransferase, glutamate 2-oxoglutarate aminotransferase, glutamate dehydrogenase, or asparaginase, whereby ectopic expression of

such a transfected gene imparts increased amino acid or nitrogen content, compared to non-transfected plants. Thus, the Examiner contends the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants respectfully disagree and submit that the teaching of the present application clearly enables one skilled in the art to make and use the presently claimed invention. The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well know in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. See *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." Phillips *Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1291 (D. Del. 1991); see also *DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985). As the cases make clear, only when there is undue experimentation is Section 112 not met. Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been explained in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *Id.*

While the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of the experiment is

not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue in *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1976):

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, . . . then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.
>
> *Id.* at 219 (emphasis in the original).

The Examiner contends that the state of the art of plant transformation with nitrogen assimilation/metabolism enzyme-encoding sequences is unpredictable. Applicants point out that they have demonstrated positive results with respect to overexpression of nitrogen assimilation/metabolism enzyme-encoding genes, i.e. faster growth and increased protein content, for plants engineered to overexpress glutamine synthetase (GS) or asparagine synthetase (AS). See Examples 6 and 7 in the present application at pages 43-64 and 68-71. In all instances, plants that exhibit ectopic overexpression of GS had enhanced growth in comparison to wild types. See page 12, lines 16-20; page 20, lines 3-10; table 2 at page 54; page 39, lines 20-25; and Figures 9 and 11.

Attention is directed to the Declaration under Section 1.132 of one of the co-inventors of the present application submitted herewith. As stated in paragraph two and shown in Exhibit A of the Declaration, Gloria M. Coruzzi is certainly one skilled in the art of plant molecular biology and biochemistry. As shown in Exhibit B and discussed in paragraph four of the Declaration, the invention is successfully applicable to other nitrogen assimilation/metabolism enzymes. In the Declaration, it is demonstrated that a glutamate 2-oxoglutarate aminotransferase (GOGAT) encoding gene was ectopically overexpressed as taught in the present application in a plant to achieve improved and enhanced growth phenotype. Thus, the results of the Applicants demonstrate that one skilled in the art can predictably make and use a trangenic plant ectopically overexpressing genes encoding nitrogen assimilation/metabolism enzymes resulting in improved growth phenotype.

The GS, AS, and GOGAT transformed plants generated according to the

teaching of the present specification by the Applicants, demonstrate that positive results can predictably be obtained using nitrogen assimilation/metabolism enzyme-encoding genes. Thus, one skilled in the art reading the teaching of the present application would predict that transformed plants could predictably be achieved, using a gene encoding aspartate aminotransferase, glutamate 2-oxoglutarate aminotransferase, glutamate dehydrogenase, or asparaginase, whereby ectopic overexpression of such a transfected gene imparts increased growth phenotype, compared to non-transfected plants under normal nitrogen conditions.

The Examiner further contends that the art of plant transformation is unpredictable due to phenomenon such as gene silencing, as exemplified by Napoli et al. and Jorgensen et al.. As admitted in the cited references, the pheonmenon was erratic and reversible. At the time, the phenomenon was not well studied and it was unclear if it was more or less pronounced in certain plants or in certain genes involved in particular pathways. With respect to plants transformed to ectopically overexpress nitrogen assimilation/metabolism enzyme-encoding genes, one skilled in the art would still expect and predict based on the references cited by the Examiner and the specification that some plants could easily be obtained that were free of the effects of such phenomena. In fact, the present specification teaches screening of plants to identify and select those that ectopically overexpress the relevant nitrogen assimilation/metabolism genes and to select those having the desired growth phenotype.

Applicants point out that although the results of the cited references suggest some variability in transgenic plants, a certain number of transgenic plants with desired characteristics were obtained without difficulty. Case law has resolved that not all embodiments of an invention need be effective. The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v E. I. Du Pont* 750 F2d. 1569. Thus, in view of Applicants results, transgenic plants ectopically overexpressing aspartate aminotransferase, glutamate 2-oxoglutarate aminotransferase, glutamate dehydrogenase, or asparaginase genes are clearly enabled by the present specificaiton.

In addition, the Examiner contends the specification fails to teach the generation of plants with increased growth, nitrogen content, or amino acid content

comprising the transfection of recombinant nucleic acids encoding nitrogen assimilation/metabolism enzymes selected from the group consisting of aspartate aminotransferase, glutamate 2-oxoglutarate aminotransferase, glutamate dehydrogenase, or asparaginase. In particular, the Examiner repeatedly contends that the specification discloses transgenic plants which grow more slowly than non-transformed plants and that one skilled in the art would therefore not consider the results of the Applicants as being correlative or representative of the successful generation of transgenic plants with improved characteristics. Applicants respectfully disagree, and draw the Examiner's attention to Table 2 on page 54 and Table 3 on page 55 of the specification wherein increase growth of transformed plants in comparison to non-transformed control plants is demonstrated. One skilled in the art would clearly correlate the positive growth data for the transgenic plants ectopically overexpressing GS or AS with the successful generation of transgenic plants with improved growth characteristics following the transfection of nucleic acids encoding aspartate aminotransferase, glutamate 2-oxoglutarate aminotransferase, glutamate dehydrogenase, or asparaginase. Applicant's data presented in the Declaration affirms that such a correlation is valid and that Applicant's data is representative of the successful generation of transgenic plants with improved growth phenotype.

The Examiner has also rejected the claimed invention on the allegation that the specification fails to teach generation of a chimeric bifunctional GOGAT enzyme. Applicants assert that generation of such an enzyme is taught in the specification at page 22, lines 22-34; Figure 2; and page 14, lines 10-24. Methods for deleting portions of and splicing nucleic acids to generate chimeric constructs are well know in the art and are disclosed at page 65, line 36 through page 66, line 20 in relation to AS constructs generated. In accordance with case law, the Applicants need not set forth every detail to meet the enablement requirement, particularly, in cases like the present where such instruction is routine, common, and readily available in the art of plant transformation. Thus, the specification sufficiently teaches one skilled in the art how to make a transgenic plant that ectopically overexpresses a nucleic acid that encodes a chimeric bifunctional enzyme having ferredoxin and NADH glutamate 2-oxoglutarate aminotransferase activities.

Further, the Examiner contends that the specification fails to provide any particular guidance for the generation of transgenic plants comprising any of the nitrogen assimilation/metabolism genes of the claimed invention and that undue experimentation would be required on the part of one skilled in the art to make and use the invention. In

particular the Examiner contends that the specification fails to disclose factors required for successful and appropriate expressing of the recombinant genes in plants whereby the desired characteristics are achieved, i.e. improved growth phenotype, or increased protein/amino acid content.

Applicants respectfully disagree. Section 5.2 of the specification at pages 23-36 teaches methods for making nucleic acid constructs and transformation into plants or plant cells. The examples provided by the Applicants using GS, AS, and GOGAT demonstrate the effectiveness of these methods and the ease with which they can be carried out. With respect to factors required for successful and appropriate expressing of the recombinant genes in plants, Applicants assert that ectopic overexpression is the appropriate expression as taught in the specification and that appropriate promoters for achieving such expression are disclosed page 24, line 34 through page 26, line 7. Moreover, identifying transgenic plants with desired characteristics is routine experimentation that can be achieved using the methods taught at page 11, line 23 through page 12, line 2, or the methods as used by the Applicants in Examples 6 and 7 for measuring plant growth phenotype and protein content.

Applicants assert that they have demonstrated one skilled in the art could use the methods disclosed in the specification for generating a transgenic plant and the methods for screening transgenic plants for desired characteristics to obtain the claimed transgenic plants of the invention. In support of this assertion Applicants submit the Declaration of co-inventor Gloria M. Coruzzi which applies the teachings of the specification to achieve the claimed transgenic plant of the invention. Applicants respectfully submit that it is not undue experimentation to make and use a transgenic plant with ectopic overexpression of a gene encoding aspartate aminotransferase, glutamate 2-oxoglutarate aminotransferase, glutamate dehydrogenase, or asparaginase, since the process of making such a plant and screening for desired phenotypes would not require a level of ingenuity beyond that which is expected by one skilled in the art.

In view of the forgoing reasoning, Applicants respectfully request the Examiner's withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

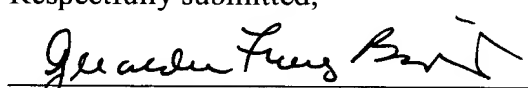
CONCLUSION

Applicants respectfully request that the present amendment and remarks be entered and made of record in the instant application. It is submitted that all the outstanding rejections have been obviated or overcome. An allowance of the application is earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

It is believed that no fee is required for filing this Amendment. In the event a fee is required, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date: April 2, 2003



31,232
(Reg. No.)

Geraldine F. Baldwin
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

enclosures

APPENDIX A

MARKED-UP VERSION OF THE AMENDED CLAIMS

U.S. Patent Application Serial No. 09/605,521

(Attorney Docket 5914-083-999)

9 (amended). The transgenic plant of claim 8, wherein the plant promoter is a strong, constitutively expressed plant promoter.

26 (amended). The [transgennic] transgenic plant of any one of claims 8, 9, 10, 21, 22, 23, or 24 wherein the transgenic and the progenitor plants thereof are selected from the group consisting of *Arabidopsis*, maize, wheat, rice, soybean, tomato, tobacco, carrots, potato, sugar beets, sunflower, yam, rape seed, and petunia.

APPENDIX B

PENDING CLAIMS

U.S. Patent Application Serial No. 09/605,521

(Attorney Docket 5914-083-999)

(as amended under 37 C.F.R. §1.111)

8. A transgenic plant having a gene construct comprising a nucleic acid encoding a nitrogen assimilation/metabolism enzyme operably linked to a plant promoter so that the nitrogen assimilation/metabolism enzyme is ectopically overexpressed in the transgenic plant, and the transgenic plant exhibits:

i) faster rate of growth,

ii) greater fresh or dry weight at maturation,

iii) greater fruit or seed yield,

iv) greater total plant nitrogen content,

v) greater fruit or seed nitrogen content,

vi) greater free amino acid content in the whole plant,

vii) greater free amino acid content in the fruit or seed,

viii) greater protein content in seed or fruit, or

ix) greater protein content in a vegetative tissue,

than a progenitor plant which does not contain the gene construct, when the transgenic plant and the progenitor plant are cultivated under identical nitrogen non-limiting growth conditions, wherein the nitrogen assimilation/metabolism enzyme is aspartate aminotransferase, glutamate 2-oxoglutarate aminotransferase, glutamate dehydrogenase, or asparaginase.

9. The transgenic plant of claim 8, wherein the plant promoter is a strong, constitutively expressed plant promoter.

10. The transgenic plant of claim 9, wherein the plant promoter is CaMV 35S promoter.

14. A seed of the transgenic plant of any one of claims 8, 9, or 10, wherein the seed has the gene construct.

15. A progeny, clone, cell line or cell of the transgenic plant of any one claims 8, 9, or 10, wherein said progeny, clone, cell line or cell has the gene construct.

21. The transgenic plant of claim 8, wherein the glutamate 2-oxoglutarate aminotransferase utilizes ferredoxin as a reductant.

22. The transgenic plant of claim 21, wherein the gene construct comprises a plant glutamate 2-oxoglutarate aminotransferase gene.

23. The transgenic plant of claim 8, wherein the glutamate 2-oxoglutarate aminotransferase utilizes NADH as a reductant.

24. The transgenic plant of claim 23, wherein the the gene construct comprises a plant or *E. coli* glutamate 2-oxoglutarate aminotransferase gene.

25. The transgenic plant of claim 8, wherein the glutamate 2-oxoglutarate aminotransferase comprises a chimeric bifunctional enzyme comprising both ferredoxin and NADH glutamate 2-oxoglutarate aminotransferase activities.

26. The transgenic plant of any one of claims 8, 9, 10, 21, 22, 23, or 24 wherein the transgenic and the progenitor plants thereof are selected from the group

consisting of *Arabidopsis*, maize, wheat, rice, soybean, tomato, tobacco, carrots, potato, sugar beets, sunflower, yam, rape seed, and petunia.